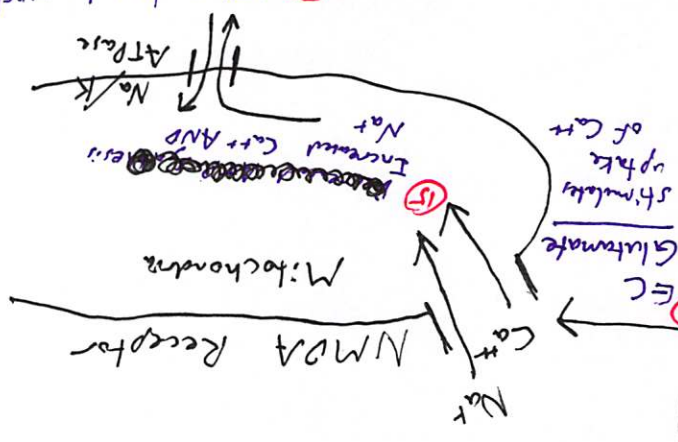
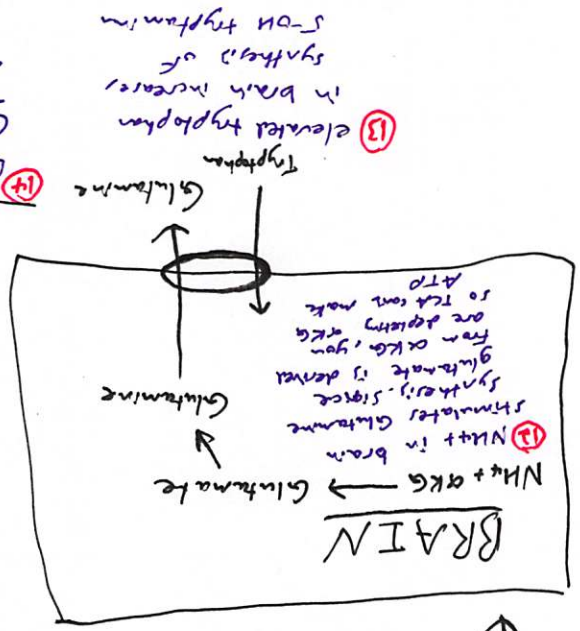
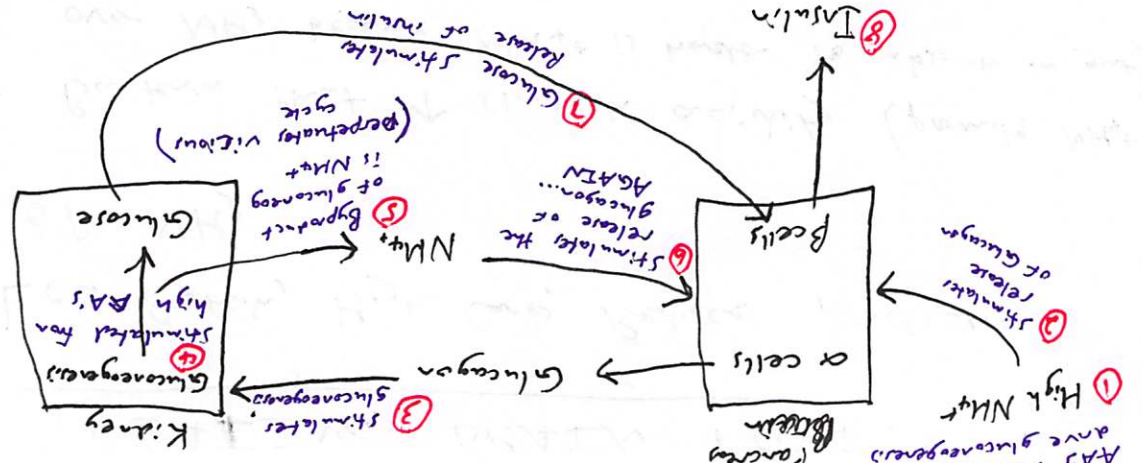


# TREATING BRAIN TOXICITY

- ① Diet - Low Protein, High Carb, Reduces production of  $\text{NH}_3$
- ② Levulose - Bacteria that  $\uparrow$  stomach acidity (promotes  $\text{NH}_4^+$  over  $\text{NH}_3$  because  $\text{NH}_4^+$  is harder to absorb in gut)  
"Concerned w/ pH LEVEL in ~~Secreta~~ Gut"
- ③ Antibiotics - Kill ammonia-producing bacteria
- ④ Sodium Benzoate - Promote Nitrogen Excretion in poop  
Sodium phenylbutyrate

# BRAIN INTOXICATION



- 1) Depletion of TCA intermediates
  - 2) Depletion of ATP
- Depletion of  $\alpha\text{KG}$  in brain which reduce TCA production
  - Depletion of INTRACELLULAR glutamate  $\Rightarrow$  can't synthesize GABA neurotransmitter
  - Increased oxidative stress due to reactive oxygen species

**MOST IMPORTANT**  
 stuff on page 2 Important Things

Alanine - usually for inter organ transportation of ammonia (amino group)

Glutamine - usually for transport of ammonia (amino group) to the liver

Metabolic Acidosis - results from the production of metabolic acids (Ketocarboxylic acids) in Diabetes is the most common example. Under these conditions urea production is suppressed (b/c  $\text{NH}_4^+$  is an acid maybe?) and consequently a lot of  $\text{N}_2$  is in the form of  $\text{NH}_4^+$ . Under these circumstances,  $\text{NH}_4^+$  is secreted directly by the kidney when you excrete ammonium. You are excreting a proton + sparing bicarbonate to form urea, so by excreting  $\text{NH}_4^+$  directly through kidney you get to save bicarbonate. This is one method of pH control!

Long term urea cycle regulation: Reflects responses to current diet: - If starved  $\Rightarrow \uparrow$  Urea Cycle Enzymes - If high protein diet  $\Rightarrow \uparrow$  urea cycle enzymes

Short-term urea cycle regulation: Carbamoyl phosphate synthetase I is allosterically stimulated (10 fold) by N Acetylglutamate. N Acetylglutamate synthetase, they depend on availability of Acetyl CoA + Glutamate. Basically, remember that if there are high levels of amino acids (meaning a lot of urea will need to be made to deal with the metabolism of the amino acids and the increased Nitrogen levels) then Urea Cycle will be turned on + stimulated.

- One way to end up w/ high levels of  $\text{NH}_3$  in the blood is if ~~you~~ you have a urea cycle disorder, in which any of the urea cycle enzymes are defective

- Another way to end up w/ high level of  $\text{NH}_3$  in the blood is if you have liver failure (from alcoholism or hepatitis)

- Why is Ammonia Toxic? - It alters the production of neurotransmitters in the brain

- Reduces intracellular ATP



